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November 24, 1998

Dr. Larry G. Hart
Board Executive Secretary
National Toxicology Program
PO Box 12233
Research Triangle Park, N.C. 27709

RE: Alcoholic beverages

Dear Dr. Hart:

This letter submits comments, sponsored by the Renewable Fuels Association (RFA), to the NTP RoC Subcommittee's upcoming evaluation of alcoholic beverages for possible listing in the *Report on Carcinogens*, and is in lieu of an oral presentation. I request that these comments be made available to the members of the Subcommittee before the meeting in early December.

RFA represents manufacturers of ethanol for non-food uses, and has an interest in NTP's review of the carcinogenic potential of alcoholic beverages. Ethanol manufactured by RFA member companies is used for, among other things, oxygenation of motor vehicle fuels, and the potential health effects of ethanol due to the public's use of oxygenated gasoline are of concern to the U.S. EPA. Given U.S. EPA's general policy of considering chemicals carcinogenic at all levels of exposure, if carcinogenic at any level, NTP's analysis of alcoholic beverages (if it decides to list them) could lead to increased concern on EPA's part about population exposures to airborne ethanol. One of my comments, therefore, addresses the applicability of epidemiologic data regarding cancer in alcohol consumers to low-dose inhalation exposures.

My second comment addresses the complex effects of alcohol consumption on health. There is mounting evidence that, in some cohorts with some patterns of alcohol consumption, alcohol has beneficial health effects. Alcoholic beverages are thus unlike many other substances and materials reviewed and listed by NTP, and the data should receive a comprehensive review.

In what follows, I expand on these two concerns.

1. Moderate alcohol consumption has demonstrated health benefits for some cohorts

The clear dangers to health and safety of excessive and/or irresponsible alcohol consumption are of enormous personal and social consequence. Special consideration of the carcinogenic effects

of chemicals and mixtures — whether encountered as occupational exposures, ambient exposures, or in foods, pharmaceuticals, or other consumer products — is a long-standing policy of many federal agencies and programs, and the wide exposure of the U.S. population to alcoholic beverages containing ethanol and many other substances merits a review of the toxicologic and epidemiologic data for alcohol. Nevertheless, it would be ironic, and of dubious public health benefit, to label or stigmatize without qualification a substance as carcinogenic, and perhaps reduce its consumption, if it has the potential to improve other aspects of health.

The carcinogenic risks of alcohol for the individual are influenced by many factors, not the least of which are age, sex, drinking habits, smoking habits, and health. Risk of morbidity or mortality from heart disease and cardiovascular disease is likewise multi-factorial. National death rates may be greatest for certain cancers or for heart disease, depending on the age, sex, and race of the cohort under study. There is significant evidence in the literature that, for some cohorts and patterns of consumption, alcohol reduces mortality from heart disease or cardiovascular disease as well as total mortality (*e.g.*, Fuchs *et al.*, 1995; Thun *et al.*, 1997). Cancer risks for the same cohorts may or may not be increased by alcohol consumption. Given that the dose-response curves for heart disease, cardiovascular disease and perhaps cancers among drinkers may be U-shaped, J-shaped, or hockey-stick-shaped, whether alcohol consumption is likely to benefit or impair health overall depends on the interaction of these curves at a particular dose.

An analysis restricted to the carcinogenic risks of alcohol consumption will not provide a full picture of alcohol's health effects or the information needed to make rational decisions about one's exposure to alcohol. Given the high degree of public anxiety surrounding cancer, classification of alcoholic beverages as carcinogenic could indeed lead individuals to reduce their consumption, even if this fails to maximize health. Therefore, although NTP's mandate may be to focus on carcinogenic effects, I urge NTP, in this unique case, to address issues of dose-response, beneficial effects, and the net health effects of consumption.

2. Carcinogenic effects of alcohol at high dose are not necessarily predictive of carcinogenic effects of ethanol at low dose

The available evidence (HEI, 1996) suggests that inhalation exposures of the general public to ethanol from gasoline are extremely low, on the order of 10 ppm (19 mg/m^3) at the gas pump for brief periods. In light of this potential for exposure, I hope that NTP will note the following points in its review of the carcinogenic activity of alcoholic beverages:

- Alcoholic beverages are usually complex mixtures of chemicals, some of which may influence the carcinogenicity of ethanol.

- Mortality rates from some cancers in some cohorts with light to moderate alcohol consumption may be *less* than in non-drinkers and heavy drinkers (Thun *et al.*, 1997; Fuchs *et al.*, 1995). It is certainly not clear, epidemiologically, whether even lower rates of alcohol consumption are associated with an increase in cancer mortality, compared to non-drinkers. The standard linear, non-threshold model of cancer risk is likely inappropriate for alcohol-related cancer.

- Alcoholic beverages typically contain about 12 g of ethanol. For a standard 70-kg person, consumption of one drink per day gives an ethanol dose of 170 mg/kg-day, while three drinks per week give a dose of 73 mg/kg-day. If exposed one hour per week to 10 ppm (19 mg/m^3) of ethanol in air, as might occur at the gas pump, the same person would receive an ethanol dose of about 0.03 mg/kg-day. These ingestion and inhalation doses are significantly different. Epidemiologic studies of drinkers do not specifically examine doses of less than one mg/kg-d.

- Ethanol is endogenously produced at low levels in the body (HEI, 1996).

Thank you for this opportunity to comment.

Sincerely,

Sarah R. Armstrong

Sarah R. Armstrong, M.S.
Senior Scientist

References

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